REMARKS/ARUGMENTS

Upon entry of this amendment, claim 1 will be amended, whereby claims 1-8, 10-18 and 20-25 will remain pending. Claim 1 is the sole independent claim.

By the amendment herein, claim 1 has been amended in accordance with amendments as discussed with the examiners during a December 14, 2005 personal interview at the Patent and Trademark Office.

Reconsideration and allowance of the application are respectfully requested.

Discussion of Interview

Applicants express appreciation for the courtesies extended by examiners Thurman Page and Isis Ghali during a December 14, 2005 personal interview with Applicant's representative Arnold Turk.

During the interview, Applicant's invention was discussed including a discussion of Oral Protein/Peptide Delivery Technology, Ver. 1.2, March 1, 2002, "Gastrointestinal Mucoadhesive Patch System (GI-MAPS™) submitted with the Supplemental Information Disclosure Statement, filed February 20, 2003. Moreover, Applicant's claimed subject matter was contrasted with Biegajski et al., U.S. Patent No. 5,700,478, and Kelm et al., U.S. Patent No. 5,686,105, and arguments were presented as to how the products disclosed in these patents were structurally different from Applicant's claimed subject matter.

Amendments to claim 1 were discussed to even more clearly set forth the structure of Applicant's invention with respect to the protecting layer, as disclosed at the bottom of page 7 of the originally filed specification. In particular, amendment of claim 1 was

discussed to clarify that the protecting layer is structured and arranged for preventing digestive juice from permeating into the drug-carrying layer and the drug-carrying layer from releasing the drug through the protecting layer.

Arguments were presented that the structure recited in amended claim 1 is patentably different from Biegajski wherein the upper layer at most slows release of the drug and is therefore not a protecting layer as recited in Applicant's claims. Moreover, it was discussed that Biegajski appears to disclose enteric layers at column 22, but these layers are not positioned as in Applicant's oral formulation.

Still further, arguments were presented that Kelm discloses an enteric polymer coating surrounding and encasing the therapeutically active agent in the unit dosage form, and is not structured and arranged as recited in Applicant's claims. The Examiners indicated that Biegajski was the closest cited art, and indicated possible withdrawal of rejection based upon Kelm.

The examiners indicated that at least claims 4 and 5 would be allowable over the prior art of record if claim 1 was further amended to include the presence of a plasticizer in the adhesion site-controlling layer, and that they would further consider all of the claims upon submission of a written response.

Response to Rejections

Claims 1-3, 6-8 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,700,478 to Biegajski et al. (hereinafter Biegajski or '478).

The rejection contends that:

> US '478 disclosed a laminated device for oral ingestion for delivering active agents into mucosa-lined body cavity such as gastrointestinal tract or rectum (abstract; col.3, lines 33-34, 49-50; col.33, lines 44-45). The device comprises adhesive layer having thickness of 5-10 mils and made of hydroxypropyl cellulose or methacrylate(both are enteric polymers), a middle polymer layer that contains the active agent loaded in there, and protective layer (col.3, lines 65-66; col.4, lines 50-67; col.7, lines 25-28; col.8, lines 66-67; col.10, lines 25-43; col.16, lines 52-65; Figure 2). The protective layer is made of polymer and wax (col.4, lines 35-45; col.10, lines 33-43). Plasticizers are included in the active agent-containing layer, i.e. permeation enhancers col.7, lines 22-35). Figure 4 shows that the adhesive layer is attached to the protecting layer as required by claim 22.

In response, Applicant notes that independent claim 1 is directed to an oral formulation for gastrointestinal drug delivery which comprises an adhesion site-controlling layer for attaching the formulation to a selected site in the intestines, a drug-carrying layer containing a drug and an adhesive to attach the drug containing layer to the selected site in the intestines when the adhesion site-controlling layer dissolves at the selected site in the intestines, and a protecting layer structured and arranged for preventing digestive juice from permeating into the drug-carrying layer and the drug-carrying layer from releasing the drug through the protecting layer, the drug-carrying layer existing between the protecting layer and the adhesion site-controlling layer, the adhesion site-controlling layer may attach to the protecting layer and the adhesion site-controlling layer is a film made of an enteric polymer, and the adhesion site-controlling layer contains a plasticizer. Thus, amongst other features, Applicant's

claims includes a drug-carrying layer between the protecting layer and the adhesion site-controlling layer which enables the oral formulation to pass through the digestive tract to a selected site in the intestines. The drug-carrying layer contains a drug and an adhesive to attach the drug containing layer to the selected site in the intestines when the adhesion site-controlling layer dissolves at the selected site in the intestines. The protecting layer is structured and arranged for preventing digestive juice from permeating into the drug-carrying layer and the drug-carrying layer from releasing the drug through the protecting layer.

To assist the Examiner's understanding of Applicant's invention, Applicant is submitting herewith a copy of a publication, Tao et al., Gastrointestinal Patch Systems for Oral Drug Delivery, Drug Discovery Today - Volume 10, Number 13, July 2005, which describes gastrointestinal patch systems including GI-MAPS of Applicant's invention.

Moreover, Applicant notes that the counterpart European, Australian and Chinese applications have been allowed for a patent in the examination for each country.

As discussed with the examiners during the above-noted interview, the rejection must establish that each and every feature recited in Applicant's claims is disclosed in Biegajski in order for there to be anticipation. In the instant situation, Applicant respectfully submits that Biegajski does not teach each and every feature recited in Applicant's claims whereby the anticipation rejection should be withdrawn.

As pointed out during the interview, the rejection contends, without any support, that hydroxypropyl cellulose or methacrylate are enteric polymers. Therefore, if the rejection is maintained, the Examiner is requested to provide documentary support for this naked assertion.

Regarding enteric polymers, it is noted that Biegajski appears to disclose enteric polymers at column 22, first full paragraph. However, this portion of Biegajski has a different structure than recited in Applicant's claims. In particular, Biegajski discloses (with emphasis added):

> A laminated device according to the invention may be bilaminate, having an adhesive layer and an active-containing layer, as shown for example in transverse sectional view in FIG. 8. Or, the device may be trilaminate, having **a third water soluble layer, poorly permeable to the active substance, interposed between the adhesive layer and the active-containing layer**, as shown for example in transverse sectional view in FIG. 9. **This layer may be made of a material such as for example polvinyl acetate ("PVAc") or ethyl cellulose, or such, for example, one of the Eudragit family of polymethacrylic copolymers commercially available from Rohm (e.g., Eudragit S100, L100, E100, L100-55)**. The Eudragit polymethacrylic copolymers are characterized by being variously soluble at various pH; Eudragit S100 has a suitably low solubility at the typical pH of the normal human saliva. The interposed third layer may where desired be made more flexible by addition of a plasticiser such as, for example, glycerine, in amount up to, for example, about 20%.

Thus, it is seen that the third water soluble layer of Biegajski is located between the adhesive layer and the active-containing layer, and does not teach Applicant's claimed subject matter.

Moreover, Biegajski discloses at column 4, lines 21-46, that:

> To a limited extent, whether or not a particular layer dissolves or disperses in the fluid milieu of the body cavity, a substance may in time move diffusionally out from the layer, so that the concentration of the substance within the layer fails. Such diffusional movement may result in release of the substance into the body cavity or, where the layer is the mucoadhesive layer, release of the substance transmucosally through the contacting mucosal surface. Or, where the particular layer is covered by an overlying layer, the substance may diffuse into and through the overlying layer. Where such diffusional release is undesirable, it may be limited by rendering the overlying layer substantially impermeable to the substance, so that release from the overlain layer is occluded until such time as the overlying layer has dissolved or dispersed. Suitably occluding layers can be constructed of a water-soluble polymer composition containing as an

> additive a nonorganic filler such as silica gel, or a fatty acid filler such as magnesium stearate, or a wax such as a paraffin, for example. For extended delayed onset, for example, a slow-dissolving substantially substance-impermeable top layer can be constructed of a hydrophobic material such as hydroxypropyl cellulose, thereby achieving a temporary occlusive (partially occlusive, at least effect. Such a modification may be made by a change in the polymer constituents of the top layer, or by introduction of additives into the layer itself.

Thus, the structure recited in Applicant's claims is not anticipates, because in Biegajski the upper layer at most slows release of the drug and is therefore not a protecting layer as recited in Applicant's claims.

Accordingly, for at least the reasons discussed above, the anticipation rejection is without appropriate basis and should be withdrawn.

Claims 1,2,6-8, 10, 12-14, 16-18, 20, 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,686,105 to Kelm et al., (hereinafter Kelm or '105).

The rejection contends that:

> US '105 disclosed dosage form for peroal administration of active agents to small intestine or colon (abstract; col.5, lines 47-52). The dosage form comprises a substrate coated with the active agent containing layer and enteric coated with at least inner and outer coating layer (abstract; col.7, lines 16-20). The substrate disclosed by the reference reads on the instantly claimed protective layer, and the enteric coating layers reads on the adhesion site controlling layer and the capsule. The active agents are included in a polymer layer (col.8, lines 21-23). The substrate is made of wax and polymer (col.8, lines 48-53; col.14, lines 50-60). Active agents to be delivered included proteins and peptides (col.6, lines 46-48). According to the disclosure of the reference, the drug containing layer is sealed between the adhesive layer and the protecting layer as required by claim 23 and also the adhesive layer and the protective layer are attached by the drug containing layer as required by claim 22.

Applicants respectfully submit that the structure disclosed by Kelm does not teach many features of Applicant's independent claim 1, including an adhesion site-controlling layer for attaching the formulation to a selected site in the intestines; a drug-carrying layer containing a drug and an adhesive to attach the drug containing layer to the selected site in the intestines when the adhesion site-controlling layer dissolves at the selected site in the intestines; or a protecting layer structured and arranged for preventing digestive juice from permeating into the drug-carrying layer and the drug-carrying layer from releasing the drug through the protecting layer; the drug-carrying layer existing between the protecting layer and the adhesion site-controlling layer; or the adhesion site-controlling layer may attach to the protecting layer and the adhesion site-controlling layer is a film made of an enteric polymer.

At the above-noted interview, it appeared that the examiners were of the opinion that this rejection may be withdrawn at least for some of the claimed subject matter. In particular, as noted above, it was discussed that Kelm discloses an enteric polymer coating surrounding and encasing the therapeutically active agent in the unit dosage form, and is not structured and arranged as recited in Applicant's claims.

Accordingly, for the reasons set forth above, this ground of rejection should be withdrawn.

Claims 4,5, 10, 11, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '478.

This ground of rejection notes deficiencies in Biegajski, but contends, without any supporting documentary evidence, that:

> The teachings of US '478 are discussed under 102 rejection above.
>
> However the reference does not teach the hemispherical shape of the protective layer, the specific drugs or the sealing of the drug-containing layer between the adhesive and protective layer.
>
> The shape of the protective layer and specific active agents does not impart patentability to the claims, absent evidence to the contrary. The sealing of the active agent-containing layer between the adhesive and the protective layers is well known in the art and widely used in the form of reservoir containing the active agent.
>
> It would have been obvious to one having ordinary skill in the ad at the time the invention was made to have the protective layer in any desired shape and select the active agent as needed with reasonable expectation of having hemispherical capsules to deliver the desired active agent to the lower part of the GIT with success.

The Examiner is reminded that a rejection is not appropriate that makes unsupported assertions that features do not impart patenability to the claimed subject matter. The rejection must establish where there is motivation in the prior art for making the asserted modification to arrive at Applicant's claimed subject matter. Accordingly, if this ground of rejection is maintained, the Examiner is requested to provide supporting documentary evidence to show motivation for making the asserted modifications to Biegajski.

Accordingly, this ground of rejection should be withdrawn.

Claims 12-18, 20, 21, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '478 in view of US 6,231,888 to Lerner et al. (hereinafter Lerner or '888).

This ground of rejection notes deficiencies in Biegajski and makes assertions, as follows:

> The teachings of US '478 are discussed under 102 rejection above.
>
> However, US '478 does not teach encapsulation of the laminate.
>
> US '888 teaches an oral device that can be in the form of multilayered composite that can be encapsulated for slow release and preferential metabolism of the delivered agent in the patient's colon (abstract; col.15, lines 65-67; col.30, lines 1-2).
>
> Therefore, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide the laminate device disclosed by US '478 to deliver active agents to the GIT, and encapsulate the device in as disclosed by US '888, motivated by the teaching of US '888 that the encapsulated device slows the release and preferential metabolism of the delivered agent in the patient's colon, with reasonable expectation of having encapsulated laminated device that deliver desired active agent to patients colon with success.

The rejection does not make up for the deficiencies noted above. Therefore, this rejection should be withdrawn for at least this reason.

Moreover, the rejection does not indicate how the primary reference is being modified with the secondary reference to arrive at Applicant's claimed subject matter. Accordingly, the rejection should be withdrawn for this additional reason.

Withdrawal of the rejection is therefore respectfully requested.

Claims 3,4, 5, 11, 15,21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over 105 to Kelm.

In this ground of rejection, the rejection is making unsupported assertions regarding the obviousness of the thickness of each layer, hemispherical shape of the protective layer, and specific drugs and shape of the protective layer.

The Examiner is once again reminded that a rejection is not appropriate that makes unsupported assertions that features do not impart patenability to the claimed subject matter. The rejection must establish where there is motivation in the prior art for making the asserted modification to arrive at Applicant's claimed subject matter. Accordingly, if this ground of rejection is maintained, the Examiner is requested to provide supporting documentary evidence to show motivation for making the asserted modifications to Kelm.

Accordingly, this ground of rejection should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejection of record, and allow each of the pending claims.

Applicant therefore respectfully requests that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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